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THE SOMATOSTATIN ANALOGUE SMS 201-995 IN LONG-TERM TREATMENT OF VIPOMA

Case Report

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Abstract. In a 60-year-old woman with an inoperable vipoma, satisfactory improvement of severe watery diarrhea was obtained over a 12-month period by subcutaneous administration of the somatostatin analogue SMS 201-995. It is suggested that SMS 201-995 may be useful in such inoperable cases, or when surgery would carry a high risk.

Key words: vipoma, somatostatin analogue.

The clinical picture of a pancreatic tumour secreting vasoactive intestinal peptide (vipoma) is dominated by diarrhoea and associated with hypokalaemia, hypochloraemia and alkalosis (2). Excess of vasoactive intestinal peptide (VIP) stimulates water secretion in the intestine and pancreas, leading to secretory diarrhoea, which may be life-threatening. The definitive treatment for vipoma is surgical removal, but the patient may present after the tumour has metastasized or when major surgery is contraindicated by poor general health. Symptomatic relief may be achieved with streptozotocin, but this drug may have unpleasant side effects (2). The following report concerns a 60-year-old woman with a pancreatic vipoma, who has received palliative treatment with a somatostatin analogue for 12 months.

CASE REPORT

A 60-year-old woman was referred with a 2 1/2-year history of profuse, watery diarrhoea. Despite relatively good appetite she had lost 15 kg in weight during the past year. On examination she had clear signs of weight loss. No intra-abdominal mass was palpable. Before admission, culture of faeces had yielded no pathologic organisms. Barium studies showed a small ulcer on the lesser gastric curvature and a normal colon, and abdominal ultrasonograms were normal.

Initial laboratory findings were as follows (normal range in brackets): Haemoglobin 7.5 mmol/l (7-10), S-potassium 2.3 mol/l (3.6-5.2), S-sodium 137 mmol/l (134-147) and

S-calcium 2.50 mmol/l (2.16-2.50). Serum creatinine, glucose and albumin levels were normal, as were those of thyroid hormones. Liver enzymes were normal apart from slightly increased alkaline phosphatase, 309 U/l (70-250). The erythrocyte sedimentation rate was 40 mm/1 h (<15). Acid-base status: pH 7.21 (7.36-7.42), PO₂ 90 mmHg (>75), PCO₂ 32 mmHg (33-47), P-bicarbonate 13.3 mmol/l (22-26) and base excess -14.5 mmol/l (-3 to +2). The platelet count was slightly increased, to 482×10⁹/l (140-350) as was the leukocyte count, to 12.9×10⁹/l (3.5-9), with normal distribution of leukocytes.

The gastric ulcer on the lesser curvature was confirmed at gastroscopy. The serum gastrin concentration was 97 pmoles/l (0-50). The patient's 24-hour stool volume was up to 14 litres, and the course was not compatible with gastrinoma. The clinical picture suggested vipoma. CT-scanning revealed enlargement of the pancreas compatible with tumour as well as metastases in the liver and retroperitoneal lymph glands (Fig. 1). Measurement of plasma VIP revealed a concentration of 190 pmoles/l (<20), compatible with vipoma. The patient was judged to be inoperable.

Treatment with the somatostatin analogue SMS 201-995 was begun with a dose of 50 µg × 2 daily by subcutaneous injection, later increased to 150 µg × 2 daily. On this regimen the stool volume was reduced to 1-2 1/24 hours. Repeat CT-scanning, after 4 months, showed no progression of the pancreatic tumour or of the metastases. Ultrasonography 10 months after the start of treatment showed unchanged tumour size. During treatment the gastrin concentration (Table I) fell from 97 to 13 pmoles/l. Contrary to expectation, the concentration of VIP did not fall, but indeed rose from 190 to 625 pmoles/l. The blood glucose profile was normal during the reported 12 months of treatment.

An attempt was made during that 12 months to discontinue treatment with the somatostatin analogue, but after 3 days the stool volume had increased to 6 1/24 hours. Resumption of treatment in the same dosage led to reduction of stool volume after 4 days to 1-2 1/24 hours.

COMMENTS

Somatostatin was first isolated from the hypothalamus in 1972 (13). It was originally thought to be a

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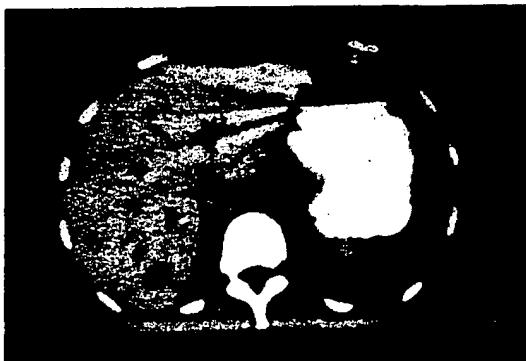


Fig. 1. CT scan showing the liver with metastasis.

specific hypothalamic factor modulating the release of growth hormone, but it is now known to have extensive effects, inhibiting the secretion of growth hormone, thyrotropin, gastrin, gut hormones, insulin and glucagon (5). Somatostatin was shown to reduce plasma concentrations of gut hormones when infused intravenously (11). These findings suggested a therapeutic use for somatostatin in non-resectable gastrointestinal endocrine tumours, but a major disadvantage was found to be the short half-life (<3 min) of somatostatin (9). Further work on somatostatin analogues with longer half-life showed that gut hormone levels and stool volume could be reduced by using the intravenous or subcutaneous route of administration (1, 4, 12, 14). Long-acting somatostatin analogues have been used for treatment of life-threatening diarrhoea (14), and in one case shrinkage of endocrine tumour was observed (7).

The mechanism of somatostatin action is not known. Increased absorption of jejunal and ileal fluid was demonstrated as well as enhanced potassium and chloride absorption and reversed sodium secretion (12). These changes did not occur when somatostatin was given to healthy controls (6). It is unlikely that somatostatin acts entirely by direct stimulation of water and electrolyte absorption in the intestine, but rather by inhibiting hormone release from the tumour or restraining the effect of secreted hormones of the intestinal mucosa.

Palliative administration of somatostatin analogues is now well recognized, but reports on their use in long-term management are few (3, 8). In our patient diarrhoea has been controlled with the hormone analogue for 12 months and no progression of

Table I. Hormone profile during treatment with SMS 201-995

Time (mo.)	VIP concentration (pmoles/l)	Gastrin concentration (pmoles/l)
0	190 (<20)	97 (0-50)
3	217	67
6	275	25
9	345	9
12	629	13

Normal values in brackets.

the tumour or of metastases in the liver and retroperitoneal lymph glands was found on CT-scan after 4 months.

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